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**A mouse model of mitochondrial disease reveals germline selection against severe mtDNA mutations.**

**Journal:** Science

**Publication Year:** 2008

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**PubMed link:** 18276892

**Funding Grants:** The Dangers of Mitochondrial DNA Heteroplasmy in Stem Cells Created by Therapeutic Cloning, Stem Cell Research Training Grant

**Public Summary:**

**Scientific Abstract:**

The majority of mitochondrial DNA (mtDNA) mutations that cause human disease are mild to moderately deleterious, yet many random mtDNA mutations would be expected to be severe. To determine the fate of the more severe mtDNA mutations, we introduced mtDNAs containing two mutations that affect oxidative phosphorylation into the female mouse germ line. The severe ND6 mutation was selectively eliminated during oogenesis within four generations, whereas the milder COI mutation was retained throughout multiple generations even though the offspring consistently developed mitochondrial myopathy and cardiomyopathy. Thus, severe mtDNA mutations appear to be selectively eliminated from the female germ line, thereby minimizing their impact on population fitness.

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